

METRONOMIC CHEMOTHERAPY

INTRODUCTION & AIMS:

Metronomic chemotherapy (MC) is an **anti-tumor therapy**. It is a conventional chemotherapy modification that uses **lower** anticancer drugs **doses** and **minor breaks** between them, so drugs are administrated daily or every few days. These changes allow to **reduce toxicity**, to avoid drug resistance and **oral administration** too.

The project objectives are showing a new and booming chemotherapy, their characteristics and to establish protocols for use thereof.

ANTITUMOR EFFECTS

Inhibition of
vasculogenesis and
angiogenesis

- ↑ Tromboespondine 1 (TSP-1)
- ↓ Ciclooxygenase 2 (COX – 2)
- ↓Tirosin Kinase (TK)

Activation of
immunity

- ↓ regulator T- Cells
- ↑ Dendritic cells
- ↑ Citotoxic T – Cells

ADVERSE EFFECTS

Grade 1

Vomiting, Anorexia, Diarrhoea, Lethargy

Grade 2

Vomiting, Anorexia, Diarrhoea,
↑ creatinine,

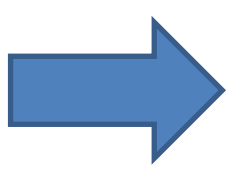
Grade 3

Neutropenia, Thrombocytopenia, Sterile
hemorrhagic cystitis

Grade 4

Hemorrhagic colitis, sterile hemorrhagic
cystitis (SHC)

Grade 5
(the most severe)



not shown

DRUGS,TUMOURS & OUTCOME IN DOGS

Drug & Dosage + Adjuvant	Tumour	Outcome
Ciclophosphamide (CYC) 12.5 – 25 mg/m ² /24h 3w + Etoposide + Piroxicam	Hemangiosarcoma	Median Survival Time (MST): 178 d. 15% SHC
CYC10 mg/m ² /24 – 48h + Piroxicam	Soft tissue sarcoma	Minimum Disease- Free interval (MDFI): 410 d. [Without MC, only surgery MDFI: 211 d]. 12% SHC
CYC 12.5 - 15 mg/m ² /24h + None	Soft tissue sarcoma	Not assessed
Chlorambucil 4mg/m ² /24h + COX inhibitors or none	transitional cell carcinoma of bladder	Stable disease (SD): 67%, Partial response (RP): 3% MST: 221d.

MOST COMMONLY USED DRUGS AND THEIR EFFECTS

Drug	Antitumor Effects
Ciclophosphamide	↑TSP-1, ↓recruitment CPEs, ↑Immune system
Non Steroidal Anti Inflammatory Drugs	↓COX
TK Inhibitors	Block TK receptors

CONCLUSIONS

Metronomic chemotherapy is not an attack therapy, it's a maintenance treatment

Experimental alternative to conventional chemotherapy against solid tumours, leukemia and metastatic tumours, with less toxicity.

New attack
targets are being
looked for

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